

REMARKS

Claims 51-59 are pending in the application and are not amended. Applicant respectfully requests reconsideration in view of the following remarks.

Claims 51-59 were rejected for alleged obviousness over Pathak (U.S. Patent 6,113,944) in view of Benneker (U.S. Patent 5,874,447) and Chu (U.S. Patent 4,675,188). Applicant respectfully traverses.

As reflected in independent claim 51, claims 51-55 are directed to pharmaceutical compositions comprising a sulfonate salt of paroxetine, calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates thereof, a disintegrant and a lubricant, wherein the compositions do not contain lactose or microcrystalline cellulose. As reflected in independent claim 56, claims 56-59 are directed to pharmaceutical compositions comprising a sulfonate salt of paroxetine, calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates thereof, a disintegrant and a lubricant, wherein the compositions have a pH within the range of 5.0 to 6.0 and an added water content of 1.2 wt% or less. Such compositions are not suggested by the cited references.

Pathak is cited for teaching paroxetine formulations with excipients such as calcium phosphate, sodium starch glycolate and magnesium stearate. Pathak discloses that microcrystalline cellulose may be absent from the formulation, and that the formulations can be formed by dry direct compression or dry granulation. As recognized in the Office Action, Pathak does not teach or suggest the use of a sulfonate salt of paroxetine or calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates. Moreover, Pathak does not teach or suggest that the paroxetine formulations should have a pH of 5.0 to 6.0.

Benneker is cited for teaching sulfonate salts of paroxetine, and for teaching that such salts exhibit greater solubility, but Benneker does not teach or suggest the use of calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates, or paroxetine formulations with a pH of 5.0 to 6.0.

Chu is cited for teaching the use of calcium hydrogen phosphate anhydrate for direct compression tableting. Chu discloses a "soft" agglomerated anhydrous dicalcium phosphate

with a specific particle size, dentin abrasion value, and surface area, but Chu does not teach or suggest that its anhydrous dicalcium hydrogen phosphate product would be particularly useful for tableting sulfonate salts of paroxetine. More importantly, Chu teaches away from the use of plate shaped crystals (or agglomerates thereof) of calcium hydrogen phosphate anhydrate as recited in the instant claims.

In column 1, Chu refers to prior art anhydrous dicalcium phosphate made by precipitation methods, referring to U.S. Patent 3,095,269. Column 2 of the '269 patent (copy attached) teaches that its anhydrous calcium hydrogen phosphate (taught to be useful as a phosphor in fluorescent lamps) "consists of plate-like crystals." Thus, the prior art anhydrous calcium hydrogen phosphate referenced in Chu includes the plate shaped crystals recited in the instant claims. Chu teaches that prior art anhydrous calcium hydrogen phosphate "cannot be used in dry direct compression as the particles are too fine and will not flow," that some prior art products "cannot meet [USP] standards without further treatment," and that some "cannot be dry granulated to make a dry direct compression tableting composition." Chu also uses some form of "precipitated" calcium hydrogen phosphate anhydrate for comparison in its examples. Thus, Chu directly teaches away from the use of calcium hydrogen phosphate anhydrate in the form of plate shaped crystals or agglomerates thereof, as recited in the instant claims.

Because the cited combination of references fails to teach or suggest each aspect of the claimed invention, and because Chu in fact teaches away from the use of the form of calcium hydrogen phosphate anhydrate recited in the claims, the Office Action fails to make out a *prima facie* case of obviousness. Accordingly, the rejection should be withdrawn.

Claims 56-59 are further distinguished from the cited references. The Office Action acknowledges that the references fail to disclose compositions with the recited pH values, but attempts to gloss over this shortcoming by asserting that it would have been obvious to adjust the relative amounts of components in order to arrive at the recited pH values to achieve optimal performance. Applicant respectfully traverses.

The Office Action states that it is obvious “to determine workable or optimal values within a prior art disclosure through the application of routine experimentation,” citing *In re Aller*. This principal is inapposite here for several reasons.

First, pH is not a parameter that is “within” any disclosure of the cited references. Pathak does not mention the pH of its formulations, and Banneker is primarily directed to specific salts, not compositions, and is likewise silent on pH. It cannot be obvious to “optimize” a parameter that is not even mentioned in the cited references.

Second, the present case presents a situation that is a far cry from *Aller*. The claims at issue in *Aller* were directed to a process for decomposing isopropyl benzene hydroperoxide by bringing the hydroperoxide into contact with sulphuric acid at a certain concentration range and at a certain temperature range. *In re Aller*, 220 F.2d 454, 455 (CCPA, 1955). The court noted that the claimed process was “identical with that of the prior art, except that appellants’ claims specify lower temperatures and higher sulphuric acid concentrations than are shown in the reference.” *Id.* Importantly, the general conditions of the process recited in the claims were disclosed in the prior art, and the recited reaction conditions were of the type that are routinely adjusted when optimizing chemical reactions. Thus, the court found that one of ordinary skill in the art would have recognized that the prior art process could be optimized, stating that “[a]ny chemist reading the [prior art reference] could logically assume that higher yields might be obtainable, and by experimentally varying conditions of temperature and acidity could find the most productive conditions.” *Id.* at 458.

Unlike *Aller*, the cited references here do not provide any indication that pH should be “optimized,” let alone that it should be controlled to be within the range of 5.0 to 6.0. As noted above, the references are silent as to the pH of their paroxetine formulations.

Moreover, unlike the predictable effects of increasing the concentration of reactants in *in vitro* chemical reactions, the cited references provide no basis for predicting that adjusting the pH of paroxetine compositions would render them more stable against discoloration, as taught in the instant specification. Thus, one of the rationales supporting obviousness in *Aller*, the notion that any chemist would “logically assume that higher yields might be

obtainable” by adjusting the experimental conditions, is not applicable here. Indeed, the record reveals no reason to make a paroxetine composition with a pH within the range of 5.0 to 6.0, as recited in claims 56-59.

Because the skilled artisan would not have arrived at the invention of claims 56-59 by “routine optimization,” the obviousness rejection is improper and should be withdrawn.

Conclusion

Applicant believes that the application is in condition for allowance, and an early notice to that effect is earnestly solicited.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance prosecution.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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